



DEPARTMENT OF THE AIR FORCE
59TH MEDICAL WING (AETC)
JOINT BASE SAN ANTONIO - LACKLAND TEXAS



15 MAR 2017

MEMORANDUM FOR SGDTT
ATTN: CAPT SARAH M RINGDAHL

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

1. Your paper, entitled **The Relationship between Fatty Liver Disease and Periodontal Disease** presented at/published to **American Academy of Dental Research (AADR) San Francisco, CA, 22 March 2017** in accordance with MDWI 41-108, has been approved and assigned local file #**17144**.
2. Pertinent biographic information (name of author(s), title, etc.) has been entered into our computer file. Please advise us (by phone or mail) that your presentation was given. At that time, we will need the date (month, day and year) along with the location of your presentation. It is important to update this information so that we can provide quality support for you, your department, and the Medical Center commander. This information is used to document the scholarly activities of our professional staff and students, which is an essential component of Wilford Hall Ambulatory Surgical Center (WHASC) internship and residency programs.
3. Please know that if you are a Graduate Health Sciences Education student and your department has told you they cannot fund your publication, the 59th Clinical Research Division may pay for your basic journal publishing charges (to include costs for tables and black and white photos). We cannot pay for reprints. If you are a 59 MDW staff member, we can forward your request for funds to the designated Wing POC at the Chief Scientist's Office, Ms. Alice Houy, office phone: 210-292-8029; email address: alice.houy.civ@mail.mil.
4. Congratulations, and thank you for your efforts and time. Your contributions are vital to the medical mission. We look forward to assisting you in your future publication/presentation efforts.

LINDA STEEL-GOODWIN, Col, USAF, BSC
Director, Clinical Investigations & Research Support

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

INSTRUCTIONS

USE ONLY THE MOST CURRENT 59 MDW FORM 3039 LOCATED ON AF E-PUBLISHING

1. The author must complete page two of this form:
 - a. In Section 2, add the funding source for your study [e.g., 59 MDW CRD Graduate Health Sciences Education (GHSE) (SG5 O&M); SG5 R&D; Tri-Service Nursing Research Program (TSNRP); Defense Medical Research & Development Program (DMRDP); NIH; Congressionally Directed Medical Research Program (CDMRP) ; Grants; etc.]
 - b. In Section 2, there may be funding available for journal costs, if your department is not paying for figures, tables or photographs for your publication. Please state "YES" or "NO" in Section 2 of the form, if you need publication funding support.
2. Print your name, rank/grade, sign and date the form in the author's signature block or use an electronic signature.
3. Attach a copy of the 59 MDW IRB or IACUC approval letter for the research related study. If this is a technical publication/presentation, state the type (e.g. case report, QA/QI study, program evaluation study, informational report/briefing, etc.) in the "Protocol Title" box.
4. Attach a copy of your abstract, paper, poster and other supporting documentation.
5. Save and forward, via email, the processing form and all supporting documentation to your unit commander, program director or immediate supervisor for review/approval.
6. On page 2, have either your unit commander, program director or immediate supervisor:
 - a. Print their name, rank/grade, title; sign and date the form in the approving authority's signature block or use an electronic signature.
7. Submit your completed form and all supporting documentation to the CRD for processing (59crdpubspres@us.af.mil). If you have any questions or concerns, please contact the 59 CRD/ Publications and Presentations Section at 292-7141 for assistance.
8. The 59 CRD/Publications and Presentations Section will route the request form to clinical investigations, 502 ISG/JAC (Ethics Review) and Public Affairs (59 MDW/PA) for review and then forward you a final letter of approval or disapproval.
9. Once your manuscript, poster or presentation has been approved for a one-time public release, you may proceed with your publication or presentation submission activities, as stated on this form. **Note:** For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.
10. If your manuscript is accepted for scientific publication, please contact the 59 CRD/Publications and Presentations Section at 292-7141. This information is reported to the 59 MDW/CC. All medical research or technical information publications/presentations must be reported to the Defense Technical Information Center (DITC). See 59 MDWI 41-108, *Presentation and Publication of Medical and Technical Papers*, for additional information.

NOTE: All abstracts, papers, posters, etc., should contain the following disclaimer statement:

"The views expressed are those of the [author(s)] [presenter(s)] and do not reflect the official views or policy of the Department of Defense or its Components"

NOTE: All abstracts, papers, posters, etc., should contain the following disclaimer statement for research involving humans:

"The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and DODI 3216.02_AFI 40-402."

NOTE: All abstracts, papers, posters, etc., should contain the following disclaimer statement for research involving animals, as required by AFMAN 40-401_IP :

"The experiments reported herein were conducted according to the principles set forth in the National Institute of Health Publication No. 80-23, Guide for the Care and Use of Laboratory Animals and the Animal Welfare Act of 1966, as amended."

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS			
1. TO: CLINICAL RESEARCH	2. FROM: (Author's Name, Rank, Grade, Office Symbol) Ringdahl, Sarah M. Capt, O-3, SGDTT	3. GME/GHSE STUDENT: <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO	4. PROTOCOL NUMBER: C.2016.016/418110
5. PROTOCOL TITLE: (NOTE: For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.) The Relationship between Fatty Liver Disease and Periodontal Disease			
6. TITLE OF MATERIAL TO BE PUBLISHED OR PRESENTED: The Relationship between Fatty Liver Disease and Periodontal Disease			
7. FUNDING RECEIVED FOR THIS STUDY? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO FUNDING SOURCE:			
8. DO YOU NEED FUNDING SUPPORT FOR PUBLICATION PURPOSES: <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO			
9. IS THIS MATERIAL CLASSIFIED? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO			
10. IS THIS MATERIAL SUBJECT TO ANY LEGAL RESTRICTIONS FOR PUBLICATION OR PRESENTATION THROUGH A COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENT (CRADA), MATERIAL TRANSFER AGREEMENT (MTA), INTELLECTUAL PROPERTY RIGHTS AGREEMENT ETC.? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO NOTE: If the answer is YES then attach a copy of the Agreement to the Publications/Presentations Request Form.			
11. MATERIAL IS FOR: <input checked="" type="checkbox"/> DOMESTIC RELEASE <input type="checkbox"/> FOREIGN RELEASE CHECK APPROPRIATE BOX OR BOXES FOR APPROVAL WITH THIS REQUEST. ATTACH COPY OF MATERIAL TO BE PUBLISHED/PRESENTED.			
<input type="checkbox"/> 11a. PUBLICATION/JOURNAL (List intended publication/journal.)			
<input type="checkbox"/> 11b. PUBLISHED ABSTRACT (List intended journal.)			
<input checked="" type="checkbox"/> 11c. POSTER (To be demonstrated at meeting: name of meeting, city, state, and date of meeting.) American Academy of Dental Research (AADR), San Francisco, CA; 22 Mar 2017			
<input type="checkbox"/> 11d. PLATFORM PRESENTATION (At civilian institutions: name of meeting, state, and date of meeting.)			
<input type="checkbox"/> 11e. OTHER (Describe: name of meeting, city, state, and date of meeting.)			
12. EXPECTED DATE WHEN YOU WILL NEED THE CRD TO SUBMIT YOUR CLEARED PRESENTATION/PUBLICATION TO DTIC NOTE: All publications/presentations are required to be placed in the Defense Technical Information Center (DTIC).			
DATE March 20, 2017			
13. 59 MDW PRIMARY POINT OF CONTACT (Last Name, First Name, M.I., email) Ringdahl, Sarah M. sarah.m.ringdahl.mil@mail.mil			14. DUTY PHONE/PAGER NUMBER 210-292-8635
15. AUTHORSHIP AND CO-AUTHOR(S) List in the order they will appear in the manuscript.			
LAST NAME, FIRST NAME AND M.I.	GRADE/RANK	SQUADRON/GROUP/OFFICE SYMBOL	INSTITUTION (If not 59 MDW)
a. Primary/Corresponding Author Chong, Chol	O-6/ Col	59 DTS/ 59 DG/ SGDTT	
b. Mealey, Brian	ret O-6		UTHSCSA Periodontics Clinic
c. Paredes, Angelo	O-4/Maj	59 MDW	
d. Magulick, John	O-4/Maj	59 MDW	
e.			
f.			
I CERTIFY ANY HUMAN OR ANIMAL RESEARCH RELATED STUDIES WERE APPROVED AND PERFORMED IN STRICT ACCORDANCE WITH 32 CFR 219, AFMAN 40-401_IP, AND 59 MDWI 41-108. I HAVE READ THE FINAL VERSION OF THE ATTACHED MATERIAL AND CERTIFY THAT IT IS AN ACCURATE MANUSCRIPT FOR PUBLICATION AND/OR PRESENTATION.			
16. AUTHOR'S PRINTED NAME, RANK, GRADE Ringdahl, Sarah, Capt, O-3		17. AUTHOR'S SIGNATURE RINGDAHL SARAH.M.1404628310 <small><i>(Digitally signed by RINGDAHL SARAH.M.1404628310 DN: cn=RINGDAHL SARAH.M.1404628310, o=AFMPC, ou=AFMPC, email=RINGDAHL SARAH.M.1404628310, c=US)</i></small>	18. DATE March 09, 2017
19. APPROVING AUTHORITY'S PRINTED NAME, RANK, TITLE CHOL H. CHONG, Col, Periodontics Flight Commander		20. APPROVING AUTHORITY'S SIGNATURE CHONG.CHOL.H.1039309889 <small><i>(Digitally signed by CHONG.CHOL.H.1039309889 DN: cn=CHONG.CHOL.H.1039309889, o=AFMPC, ou=AFMPC, email=CHONG.CHOL.H.1039309889, c=US)</i></small>	21. DATE March 09, 2017

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS			
1st ENDORSEMENT (59 MDW/SGVU Use Only)			
TO: Clinical Research Division 59 MDW/CRD Contact 292-7141 for email instructions.	22. DATE RECEIVED March 09, 2017	23. ASSIGNED PROCESSING REQUEST FILE NUMBER 17144	
24. DATE REVIEWED March 14, 2017		25. DATE FORWARDED TO 502 ISG/JAC	
26. AUTHOR CONTACTED FOR RECOMMENDED OR NECESSARY CHANGES: <input type="checkbox"/> NO <input checked="" type="checkbox"/> YES If yes, give date. <u>March 13, 2017</u> <input type="checkbox"/> N/A			
27. COMMENTS <input checked="" type="checkbox"/> APPROVED <input type="checkbox"/> DISAPPROVED IRB approved dental presentation with appropriate disclaimers. Approved			
28. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER Kevin Kupferer/GS13/Human Research Subject Protection Expert		29. REVIEWER SIGNATURE KUPFERER KEVIN R.1086667270 <small>Digitally signed by KUPFERER KEVIN R.1086667270 DN: cn=KUPFERER KEVIN R.1086667270, ou=502 ISG/JAC, email=kupferer.kevin@us.af.mil, c=US Date: 2017.03.14 16:34:50 -0500</small>	30. DATE March 14, 2017
2nd ENDORSEMENT (502 ISG/JAC Use Only)			
31. DATE RECEIVED		32. DATE FORWARDED TO 59 MDW/PA	
33. COMMENTS <input type="checkbox"/> APPROVED (In compliance with security and policy review directives.) <input type="checkbox"/> DISAPPROVED			
34. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER		35. REVIEWER SIGNATURE	36. DATE
3rd ENDORSEMENT (59 MDW/PA Use Only)			
37. DATE RECEIVED March 14, 2017		38. DATE FORWARDED TO 59 MDW/SGVU March 14, 2017	
39. COMMENTS <input checked="" type="checkbox"/> APPROVED (In compliance with security and policy review directives.) <input type="checkbox"/> DISAPPROVED			
40. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER Kevin Iinuma, SSgt/E-5, 59 MDW Public Affairs		41. REVIEWER SIGNATURE IINUMA KEVIN MITSUGU.1296227 <small>Digitally signed by IINUMA KEVIN MITSUGU.1296227 DN: cn=IINUMA KEVIN MITSUGU.1296227, ou=59 MDW/PA, email=iinuma.kevin@us.af.mil, c=US Date: 2017.03.14 16:17:00 -0500</small>	42. DATE March 14, 2017
4th ENDORSEMENT (59 MDW/SGVU Use Only)			
43. DATE RECEIVED		44. SENIOR AUTHOR NOTIFIED BY PHONE OF APPROVAL OR DISAPPROVAL <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> COULD NOT BE REACHED <input type="checkbox"/> LEFT MESSAGE	
45. COMMENTS <input type="checkbox"/> APPROVED <input type="checkbox"/> DISAPPROVED			
46. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER		47. REVIEWER SIGNATURE	48. DATE



The Relationship Between Fatty Liver Disease and Periodontal Disease



S. Ringdahl^{1,2}, C. Chong¹, B. Mealey², A. Paredes³, J. Magulick³

¹United States Air Force Post Graduate Dental School, Periodontics, San Antonio, Texas

²The University of Texas Health Science Center at San Antonio, Department of Periodontics

³San Antonio Military Medical Center, Hepatology Clinic, San Antonio, Texas



#0980

ABSTRACT

Periodontitis is a highly prevalent and destructive chronic disease. Numerous studies support an association between periodontal disease and other systemic diseases (diabetes, cardiovascular disease, chronic kidney disease, adverse pregnancy outcome, etc.). Non-alcoholic fatty liver disease (NAFLD) is a chronic inflammatory disease that is characterized by accumulation of triglycerides and fat in the liver which may lead to fibrosis and even cirrhosis. The mechanism of this destruction is due to activation of inflammatory cells and upregulation of cytokines, much like the chronic inflammatory destruction seen in periodontal disease. The association between these two diseases has never been investigated. A reasonable mechanism in which periodontal disease may play a role in the destruction seen in NAFLD is the remote site infection of periodontal disease. Chewing and oral hygiene measures lead to systemic release of bacterial byproducts and subsequent systemic inflammatory response which may subsequently lead to the changes seen in the liver. **Objective:** The purpose of this cross-sectional study is to investigate the relationship between periodontal disease and NAFLD.

MATERIALS and METHODS

Liver diagnosis and blood draw: Patients with a diagnosis of NAFLD determined from previous liver biopsy were recruited for this study. Patients were seen at the hepatology clinic for informed consents and blood draw for cytokine panel and liver enzyme assay (including aspartate aminotransferase (AST) and alanine aminotransferase (ALT)). Patients were subsequently scheduled at the dental clinic for periodontal examination. Liver diagnoses were categorized based on severity of cirrhosis with stage 1 and 2 having no cirrhosis and stage 3 and 4 having cirrhosis.

Periodontal examination: Full mouth periodontal examinations were completed by a single examiner (S.R.) who remained blinded to liver diagnosis until after data entry. A UNC-15 probe was used to measure probing depths (PD) and clinical attachment level (CAL) on 6 sites/tooth. Sites with bleeding were also recorded at 6 sites/tooth. Plaque index was measured at 4 sites/tooth following use of disclosing agent. Third molars were excluded from examination. Severity of periodontal disease was defined as mean PD and mean CAL. Extent of PD was determined by the percentage of sites having ≥ 3 mm CAL and percentage of sites having PD of 5mm or greater. Periodontal diagnosis was made using the CDC-AAP periodontal disease criteria as mild (defined as ≥ 2 interproximal sites having ≥ 3 mm CAL and ≥ 2 interproximal sites with PD >3 mm not on the same tooth, or ≥ 1 site with ≥ 5 mm PD), moderate (defined as ≥ 2 interproximal sites having ≥ 4 mm CAL or ≥ 2 interproximal sites with PD ≥ 5 mm not on the same tooth), or severe (defined as ≥ 2 interproximal sites having ≥ 6 mm CAL and ≥ 1 interproximal site with PD ≥ 5 mm).

Exclusion criteria: Patients with less than 12 teeth, co-existing autoimmune disorders, currently taking antibiotics, or pregnant/breast feeding women were excluded from the study. Additionally, patients who did not take recommended antibiotic prophylaxis were excluded. Patients were not excluded for having diabetes or for current tobacco use.

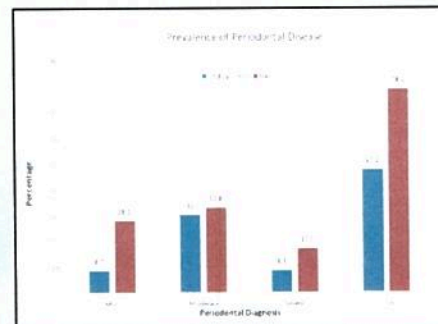
Statistical Analysis: Demographic data was analyzed using mean values and ranges. Statistical analyses were made using Spearman Rank correlation. Significance was defined by a $p < 0.05$.

RESULTS

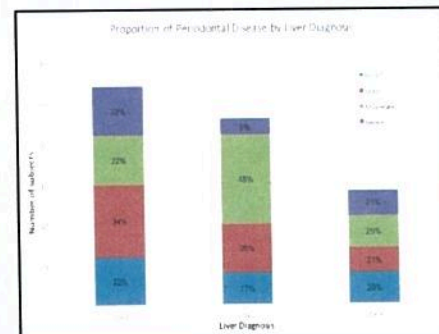
A total of 64 patients have completed the liver biopsy and periodontal exam portions of this research project and were included in data analysis. The mean age for included patients was 56 years (range 32-79). Male patients comprised 67% of our population. The average number of teeth per patient was 25.45 (range 15-28).

None of the patients included in this study were current smokers, however, 28% were former smokers. Average BMI was 33.3 (range 24-44.3). 54% of the subjects had diagnosis of type II diabetes mellitus.

Of the patients completing study protocol (a total of 64) 78% of included patients had some degree of periodontal disease, with 28% having mild, 33% having moderate, and 17% having severe periodontal disease (See graph below.)



When evaluating the breakdown of periodontal disease severity by liver diagnosis, in the group with fatty liver disease without cirrhosis (LDx1), 78% had some degree of periodontal disease, with 34% being mild, 22% moderate, and 22% having severe periodontal disease. In the patients with mild liver cirrhosis, 83% had some degree of periodontal disease, with 26% having mild, 48% having moderate, and 9% having severe disease. In the group of patients with more extreme liver cirrhosis, 71% had some form of periodontal disease with 21% having mild, 29% having moderate, and 21% having severe disease (see graph below).



The Spearman rank correlation coefficient reached significance when comparing AST and ALT values to the periodontal diagnosis [AST: -0.33 ($p=0.02$) and ALT: -0.43 ($p=0.002$)] and the presence or absence of periodontal disease [AST: -0.28 ($p=0.047$) and ALT: -0.34 ($p=0.01$)]. ALT values were also inversely related to the percentage of sites with ≥ 3 mm CAL [-0.29 ($p=0.04$)].

The statistical analysis of the liver diagnosis to the various periodontal disease measures of extent and severity (percentage of sites with PD ≥ 5 mm, percentage of sites with CAL ≥ 3 mm, mean PD, mean CAL, bleeding index, and plaque index), found none of the correlation coefficients to be significant.

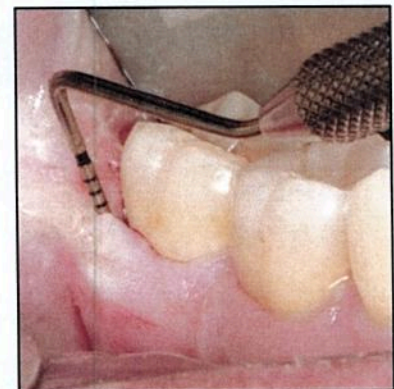
DISCUSSION

In a preliminary data analysis of this cross-sectional study evaluating the relationship between periodontal disease and non-alcoholic fatty liver disease, there was no statistical relationship between severity of NAFLD and periodontal disease severity or extent.

A statistically significant inverse relationship between periodontal disease diagnosis and AST and ALT values was seen. A significant inverse relationship with ALT value and percentage of sites with ≥ 3 mm CAL was also seen.

Although our number of subjects is too small to draw conclusions in regard to prevalence, there appears to be a larger proportion of periodontal disease in this population of patients with NAFLD than in the general US population.

Continued research will focus on increasing number of subjects and analyzing specific inflammatory cytokine values (IL-1, IL-6, IL-8, TNF- α , CRP), CD4:CD8 ratio and presence or absence of CMV antibodies to the severity of periodontal disease and NAFLD.



REFERENCES

- Mealey B and Oates T. Diabetes mellitus and periodontal diseases. J Periodontol 2006; 77: 1289-1303.
- Eke PI, Dye BA, Wei L, Thornton-Evans GO, Genco RJ. Prevalence of Periodontitis in Adults in the United States: 2009 and 2010. J Dent Res 91(10): 914-920, 2012
- Demir, M, Lang, S, and Steffen HM. Nonalcoholic fatty liver disease: Current Status and future directions. Journal of Digestive Diseases. 2015. DOI: 10.1111.1751-2980.12291.
- Chalasani, N., Younossi, Z., Lavine, J. E., Diehl, A. M., Brunt, E. M., Cusi, K., Sanyal, A. J. (2012). The diagnosis and management of non-alcoholic fatty liver disease: Practice guideline by the american association for the study of liver diseases, american college of gastroenterology, and the american gastroenterological association. American Journal of Gastroenterology, 107(6), 811-826. doi:10.1038/ajg.2012.128
- Williams, CJ et al. Prevalence of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among a largely middle-aged population utilizing ultrasound and liver biopsy: a prospective study. Gastroenterology. 2011 Jan;140(1):124-31.

DISCLAIMER

The opinions expressed in this poster are solely those of the author(s) and do not represent an endorsement by or the views of the United States Air Force, the Department of Defense, or the United States Government